

Prebiotic Peptide Synthesis

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About four billion years ago on the primitive Earth, chemical processes yielded molecules that had the ability to make copies of themselves (self-replicate). Over evolutionary time, these replicating molecules developed into the deoxyribonucleic acid (DNA) protein-replicating system of modern life. Although the DNA molecule has a structure that makes it an excellent self-replicating molecule, its structure is too complex to have been synthesized by chemical processes on the early prebiotic Earth. This difficulty with the prebiotic synthesis of DNA has led to a search for simpler replicating molecules. One of the best candidates for a primitive replicating molecule is a small protein, called a peptide. Peptides are considered good candidates because they are constructed from very simple building blocks—activated amino acid molecules—that could have been made by chemical processes on the primitive Earth. To understand the prebiotic processes on the early Earth that could have generated replicating molecules, such as peptides, this study has examined plausible prebiotic chemical processes that have the potential to yield peptides and other replicating molecules from very simple chemical ingredients such as formaldehyde and derived sugars, and analyzed the thermodynamics of carbon chemistry to establish which types of organic reactions are energetically favorable or unfavorable under mild aqueous conditions.

Because earlier studies have indicated the involvement of amino acid and peptide thioesters in prebiotic peptide synthesis, a new, very simple method for preparing peptide

thioesters was developed; this method involves the reaction of a thiol molecule with amino acids activated by reaction with the commercially available reagent (carbonyldiimidazole). This synthetic method was used to prepare peptide thioesters from three and eight amino acids in length for several different amino acids. Chromatographic techniques were developed that allow measurement and purification of the peptide thioesters. This new synthetic method provides an uncomplicated way to generate peptide thioesters for studies of peptide replication.

To identify and understand the chemistry that could have been involved in the origin of the earliest replicating molecule under mild aqueous conditions, the energy values for the chemical changes that occur in carbon groups undergoing redox reactions and carbon-carbon bond cleavage reactions were calculated. Results indicate that the energy of redox reactions involving hydrogen transfer between carbon groups is determined mainly by the type of functional group that donates the hydrogen equivalents, with the energy becoming less favorable in the order: aldehydes, formic acid, alcohols, and hydrocarbons. In addition, results indicate that the cleavage energy of carbon-carbon bonds is determined primarily by the type of functional group that donates the shared electron-pair during cleavage, with the cleavage energy becoming less favorable in the order: carbonyls (ketones, aldehydes), carboxylic acids, alcohols, and hydrocarbons; and that the cleavage energy is more favorable when the shared electron-pair is transferred from a more oxidized to a more reduced carbon group,

except for bonds between a carbonyl group and a carboxylic acid group where the reverse transfer is more favorable. From the energy of each cleavage reaction, the energy of its corresponding synthesis (or reverse) reaction that has an energy equal to the negative of the cleavage energy was estimated. Results indicate that the chemistry of the origin of life and the structure of metabolism are constrained

and limited by the strong dependence of the energy of carbon group transformations on the type of functional group(s) participating in the transformations.

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